

REMARKS

Claims 1, 3-9, 11-14, 19, 21-24, 27, 29, 37, 39-45, 47-50, 55, 57-60, 63, 65 and 91-100 were pending. Claims 1, 5, 12-14, 19, 37, 41, 48-50, 55, 94 and 99 are amended, and claims 11, 21-22, 47, 57-58, 91, 93, 96 and 98 are cancelled without prejudice, by this Amendment. No new matter has added. The applicant respectfully requests reconsideration of the pending claims in light of the above amendments and the following remarks

1. Rejections under Section 102

Claims 1, 3-7, 11-14, 19, 21-24, 27, 29, 37, 39-45, 47-50, 55, 57-60, 63, 65 and 91-100 were rejected under 35 U.S.C. § 102(e) as allegedly being anticipated by U.S. Patent No. 6,165,778 (“Kedar”). Claims 11, 21-22, 47, 57-58, 91, 93, 96 and 98 have been cancelled without prejudice, rendering the rejection moot as applied to those claims; with respect to the remaining claims, the applicant respectfully disagrees.

a. Claims 1, 3-7, 12-14, 37, 39-45, and 48-50

Claim 1 is directed to a computer-implemented method for generating a library design, in which a user inputs a plurality of mappings defining distribution patterns that assign chemicals or chemical mixtures to cells in a destination arrangement. A first mapping defines a gradient distribution pattern for assigning a first chemical or mixture to a plurality of destination cells, where the gradient pattern is specified according to minimum and maximum amounts of the first chemical or mixture to be assigned to any of the plurality of cells, and a gradient to be applied between the minimum and maximum amounts. As amended, the claim specifies that a second mapping defines a second distribution pattern that describes an amount or amounts of a second chemical or mixture to be distributed to selected cells in the destination arrangements. The claim further specifies that the selected cells of the second mapping include one or more of the plurality of cells of the first mapping – that is, there is some overlap between the cells of the first and the second mappings. Both mappings are then used to determine amounts of the first and second chemicals or mixtures that will be deposited in the overlap area, and a visual representation of the destination arrangement is modified to include an indication of the determined amounts of the first and second chemicals or mixtures. Support for the

amendments can be found, *inter alia*, at page 2, lines 20-32, page 16, lines 11-27, page 19, lines 1-29, and original claims 11-13,.

Kedar discloses “[a] device and methods for synthesizing diverse molecular products on substrates”. *See* Kedar, Abstract. The reference discloses techniques for synthesizing peptides and oligonucleotides on microscopic beads to generate libraries “composed of many beads, each of which contains many copies of a single peptide (with a defined sequence) and a single-stranded DNA tag whose sequence artificially and unambiguously codes for the structure of the associated peptide”. *Id.*, column 4, lines 54-63. More specifically, Kedar describes variations of a synthetic technique known as “pooling”, whereby diverse compounds are prepared on solid supports by randomly distributing the supports among a set of reaction vessels, exposing the supports in each vessel to a common building block, combining (or “pooling”) the supports into a common reservoir, randomly redistributing the supports among the reaction vessels (such that a given reaction vessel will contain a different collection of supports in the second round than in the first round), again exposing the supports in each vessel to chemical building blocks to add the new building block to the growing compound on the support, and repeating the pooling, distributing, and exposing steps, until the compound on each support has reached a desired length. *See, e.g.*, column 5, lines 5-20.

However, Kedar fails to disclose at least the claimed steps of receiving first user input defining a first mapping that defines a gradient distribution pattern for a first chemical or mixture of chemicals and second user input defining a second mapping defining a second distribution pattern for a second chemical or mixture of chemicals, using the first mapping and the second mapping to determine amounts of the first and second chemicals or mixtures of chemicals to be deposited in selected destination cells, and modifying a visual representation of one or more destinations to include a visual indication of determined amounts of the first and second chemicals or mixtures of chemicals.

Regarding the mappings, the Examiner first cites a passage at column 93, lines 8-14 of Kedar as allegedly disclosing that the Kedar system is “based on receiving user input”. However, although this passage does state that a user may configure the Kedar system by means of so-called “CFG files”, it does so in the context of associating valves

with reaction vessels (“The system loads the appropriate files to inform which are the appropriate valves to use. In effect, CFG files map or ‘associate’ the valves with each selected reaction vessel.”). Nothing in the cited passage discloses using such files to define first and second distribution patterns for assigning amounts of components to destination locations as the present claims require.

Next, the Examiner cites a passage that appears at column 92, lines 5-13 of Kedar, again as allegedly disclosing a system based on receiving user input. Here, the cited passage describes the use of an “Open/Pulse” command that can be used to fill or drain a selected group of reaction vessels for a predefined time period. *See* Kedar, column 91, line 66 to column 92, line 1. In this context, the cited passage merely discloses that the user can select a group of valves to be activated during the fill or drain operation, and specify the time period for which the valves are to remain open during the operation. But while this passage may disclose that a user may interact with the Kedar system to select and configure valves during the filling and draining of reaction vessels, it, too, fails to disclose the receipt of input defining first and second distribution patterns for assigning amounts of components to destination locations as the present claims require.

The Examiner then cites passages at column 5, lines 21-35 and column 34, lines 25 to 48 of Kedar as allegedly disclosing “different optional percentages [that] reflect a minimum and a maximum”. The passages in question describe a particular improvement relating “to the chemistry used to remove the Fmoc protecting group from the alpha-amino group of a bead, linker or growing peptide chain” in solid-phase peptide synthesis. *See, e.g.*, Kedar, column 5, lines 23-26. The Examiner emphasizes the statement in the first passage that “Preferably, such removal is effected by treatment with 5 to 15%, preferably 10%, piperidine for 5 to 60 minutes, although other conditions may be employed, e.g., 15 to 30% piperidine for 5 to 30 minutes” (*id.*, lines 26-30), and that “Other improvements relate to the activation chemistry of the peptide coupling reactions, in that when certain automated instrumentation is used to perform synthesis of an oligonucleotide tagged peptide library, the invention provides for a simple mixture of HOBt/HBTU to reduce reagent supply bottles” (*id.*, lines 30-35).

But as the second cited passage makes clear, the “minimum and maximum” identified by the Examiner merely describes a range of suitable concentrations of

piperidine solution that can be used in a deprotection reaction in Kedar's solid-phase peptide synthesis. *See, e.g.*, Kedar, column 34, lines 25-33 (noting, in the context of removal of the amino-terminal Fmoc protecting group from a linker or peptide, that "Typically, treatment with 30% piperidine in DMF for about one hour is used to achieve this deprotection (see also step 8), but one aspect of the present invention relates to the use of reduced concentrations of piperidine or reduced deprotection times for the synthesis of oligonucleotide tagged peptide libraries"). Nowhere does the reference disclose the assignment of amounts (or concentrations) of piperidine solution to a plurality of destination cells according to a user-defined distribution pattern. Nor does the reference disclose such a pattern that defines a varying piperidine concentration across a plurality of destination cells according to a minimum value, a maximum value, and a gradient between the two.

Finally in the context of mappings, the Examiner also cites a passage at column 14, lines 17 to 24 of Kedar as allegedly disclosing "the idea of possibly different amounts in different destinations and all combinations thereof". But the cited passage merely discloses that the members of a chemical library may contain different combinations of different monomers – for example, a set of X^n different compounds representing all possible combinations of X different monomers to form oligomers n units long. Kedar, column 14, lines 18-21 ("all combinations of X different monomers in a set of monomers assembled into length n oligomers, yielding X^n different compounds"). Although this may disclose varying the identity of the monomers used at each stage of the synthesis, or the order in which the monomers are assembled, the applicant respectfully submits that it does not disclose varying the amounts of components used at different locations as the present claim requires.

Turning to the claimed use of the mappings, the Examiner cites a passage at column 9, lines 15 to 20 of Kedar as allegedly disclosing "the possible gradient the user may select for filling the different reaction vessels". But here, the cited passage (and referenced figures) merely show the use of dialog boxes to select reaction vessels to be used in a synthesis, a sequence of macros that define a synthetic procedure, and symbols representing the amino acid and oligonucleotide tag to be associated with each reaction vessel. *See* Kedar, column 9, lines 15 to 20 & Figures 42 to 44. Nothing in the cited

passage or figures discloses any gradient distribution pattern whatsoever, much the use of such a distribution pattern, in combination with a second mapping, to determine amounts of first and second chemicals or mixtures to be deposited in selected destination cells.

Finally, the Examiner cites this same short discussion of Figures 42 to 44 in the context of modifying the visual representation, stating that the passage shows “After the user selects the vessels and corresponding amounts of chemical to be added the GUI reflects the change in the visualization representation”. But as noted above, nothing in the cited passage, or indeed the reference as a whole, discloses the receipt of input defining first and second distribution patterns for assigning amounts of components to destination locations in general, the specific receipt of a gradient distribution pattern in such input, or the use of such distribution patterns to determine amounts of chemicals or mixtures to be deposited in selected destination cells. As such, although Figure 44 may disclose a dialog box in which the user can supply symbols that represent monomers and tags to be associated with selected reaction vessels, the reference does not disclose modifying a visual representation of a defined destination to include an indication of amounts of such chemicals or mixtures that are determined based on such distribution patterns.

Because Kedar thus fails to disclose at least these limitations of claim 1, the reference cannot anticipate that claim under 35 U.S.C. § 102(e). Claims 3-7 and 12-14 are dependent claims based directly or indirectly on claim 1, and therefore include all of the limitations of that claim. Claims 37, 39-45, and 48-50 are computer program product claims that include limitations directly analogous to those recited in method claim 1. The applicant respectfully submits that Kedar cannot anticipate any of these claims for at least the reasons discussed above in the context of claim 1. The rejection under Section 102(e) should therefore be withdrawn as to these claims.

b. Claims 19, 23-24, 27, 29, 55, 59-60, 63, 65, 92, 94-95, 97 and 99-100

Like claim 1, claim 19 is directed to a computer-implemented method for generating a library design for a library of materials. Unlike claim 1, the method of claim 19 includes steps of receiving user input that specifies a plurality of equations, and that associates one or more sources and the plurality of equations with one or more destination areas in a visual representation. The equations are solved to calculate

amounts of one or more first source chemicals or mixtures of chemicals to be assigned to cells in the destinations, and the visual representation of the destinations is modified to include a visual indication of the calculated amounts. As amended, the claim specifies that the chemical or mixture to be assigned to a given cell is determined by the source or sources associated with the destination area or areas that include the cell, and the amounts of that chemical or mixture of chemicals to be assigned to that cell are calculated according to the equations that are associated with the destination area or areas that include the cell. Support for the amendments can be found at page 20, lines 1 to 20, page 21, line 21 to page 22, line 31, page 23, lines 26 to 30, and page 24, line 26 to page 25, line 19 of the specification, as well as original claims 21, 22, 26 and Figures 7A-7C and 8A-8B.

Regarding the claimed use of equations, the Examiner appears to cite various passages and figures of Kedar, including column 5, lines 5-20, Figure 33, columns 14-18, Figures 19A and 19B, columns 5-8, and column 36, lines 38-68. However, the applicant respectfully submits that Kedar fails to disclose at least the claimed steps of receiving input specifying a plurality of equations and associating each of the plurality of equations with one or more of the destination areas, solving the equations to calculate amounts of one or more chemicals or mixtures to be assigned to one or more destination cells, where the amounts of chemicals or mixtures to be assigned to a given cell are calculated according to a set of equations that are associated with the destination area or areas that include the cell and the chemicals or mixtures to be assigned to the given cell are determined by the sources associated with the area or areas that include the cell, and modifying the visual representation of the destinations to include a visual indication of the calculated amounts. Thus, for example, nothing in the cited passages, or indeed the reference as a whole, discloses that a user of the Kedar system can provide an input that specifies an equation of any kind, or that associates such an equation with one or more areas of a destination. Likewise, Kedar also fails to disclose the step of calculating amounts of one or more chemicals or mixtures to be assigned to a given destination cell by solving a set of equations that are associated with a destination area or areas that include the given cell, or modifying a visual destination representation to include an indication of such calculated amounts.

Because Kedar fails to disclose at least these limitations of claim 19, the reference cannot anticipate that claim under 35 U.S.C. § 102(e). Claims 23-24, 27, 29, 92 and 94-95 are dependent claims based directly or indirectly on claim 19, and therefore include all of the limitations of that claim. Claims 55, 59-60, 63, 65, 97 and 99-100 are computer program product claims that include limitations directly analogous to those recited in method claim 19. The applicant respectfully submits that Kedar cannot anticipate any of these claims for at least the reasons discussed above in the context of claim 19. The rejection under Section 102(e) should therefore be withdrawn as to these claims.

2. Rejections under Section 103

Claims 1, 3-9, 11-14, 19, 21-24, 27, 29, 37, 39-45, 47-50, 55, 57-60, 63, 65 and 91-100 were rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over U.S. Patent No. 6,044,212 (“Flavin”) in view of U.S. Patent No. 6,044,617 (“Schultz”) and U.S. Patent No. 6,295,514 (“Agrafiotis”). Claims 11, 21-22, 47, 57-58, 91, 93, 96 and 98 have been cancelled without prejudice, rendering the rejection moot as applied to those claims; with respect to the remaining claims, the applicant respectfully disagrees.

a. Claims 19, 23-24, 27, 29, 55, 59-60, 63, 65, 92, 94-95, 97 and 99-100

As noted above, amended claim 19 recites a computer-implemented method of generating a library design in which user input specifies a plurality of equations and associates those equations with one or more destination areas in a visual representation. The equations are solved to calculate amounts of one or more first source chemicals or mixtures of chemicals to be assigned to cells in the destinations, and the visual representation of the destinations is modified to include a visual indication of the calculated amounts. Significantly, the claim specifies that the amounts of one or more first chemicals or mixtures of chemicals to be assigned to given cell are calculated according to a plurality of the equations that are associated with the destination area or areas that include the cell. In other words, the claim specifies that multiple equations are associated with a destination area or areas that include the given cell, and that these multiple equations are used to calculate the amounts of one or more first chemicals to be assigned to the given cell.

Even assuming that the cited references can be combined to disclose some form of computer-implemented tool for designing a library of materials, none of the references, alone or in combination, discloses or suggests any method or system in which user input specifies a plurality of equations and associates each of those equations with a destination area or areas. Nor do any of the references, alone or in combination, disclose or suggest calculating amounts of chemicals or mixtures to be assigned to particular destination cells according to a plurality of user-specified equations that are associated with destination areas that include those cells.

Because the cited combination of references fails to disclose or suggest at least these limitations of claim 19, no *prima facie* showing of obviousness has been established with respect to that claim, or to claims 23-24, 27, 29, 55, 59-60, 63, 65, 92, 94-95, 97 and 99-100, which include the same or analogous limitations as discussed above. The applicant therefore respectfully requests that the rejection under Section 103 be withdrawn as to these claims.

b. Claims 1, 3-9, 12-14, 37, 39-45, and 48-50

Similarly, and as noted above, amended claim 1 is directed to a computer-implemented method for generating a library design, in which a visual representation of a destination arrangement is displayed, amounts of chemicals or mixtures to be assigned to particular cells of a destination arrangement are determined using multiple user-supplied mappings that are associated with the cells, and the determined amounts are presented to the user by modifying a visual representation of the destination arrangement to indicate the amounts. More specifically, the amounts are determined using first and second mappings input by the user that define overlapping distribution patterns, including a gradient distribution pattern, describing amounts of chemicals or mixtures to be deposited in a particular cell or cells.

The Examiner cites Agrafiotis as apparently disclosing a generic user interface for combinatorial library design (Office action at pp. 10-11). But Agrafiotis is directed not to some generic notion of “computer design of a set of compounds”, as the Examiner suggests, but to techniques “for visualizing and interactively analyzing data relating to chemical compounds.” Agrafiotis, Abstract. According to the reference, a user selects a set of compounds to be analyzed and a method for evaluating the similarity or

dissimilarity between the selected compounds. *Id.* The system generates a “non-linear map” that represents the set of compounds. *Id.*; *see also id.*, column 2, lines 15-19. This non-linear map includes a point representing each of the selected compounds, where the “distance between any two points is representative of similarity/dissimilarity between the corresponding compounds.” *Id.*, column 2, lines 19-23. The “map” is displayed to the user, who can then interactively examine how the compounds are similar or different. *Id.*, column 2, lines 23-26.

Agrafiotis thus describes using non-linear mapping techniques to “visualize[e] proximity relations of objects by distances of points in a low-dimensional Euclidean space” (*id.*, column 6, lines 63-65) – that is, to measure distances between compounds in a “similarity” space, based on structural, chemical, physical or biological properties of the compounds (*see e.g., id.*, column 10, lines 32-38) – while the present claims “map” components in the sense of assigning amounts of the components to destination cells that represent physical locations at which materials can be prepared. Nothing in Agrafiotis (or, for that matter, Flavin or Schultz) would suggest to one skilled in the art that the non-linear mapping techniques used to represent the similarity/dissimilarity of selected properties of different compounds in Agrafiotis would be appropriate for use in assigning amounts of materials to physical library locations as contemplated by the present claims. The applicant therefore submits that no *prima facie* showing of obviousness has been established with respect to claims 1, 3-9, 12-14, 37, 39-45, and 48-50, and respectfully requests that the rejections under Section 103 be withdrawn as to these claims as well.

3. Rejections for Obviousness-Type Double Patenting

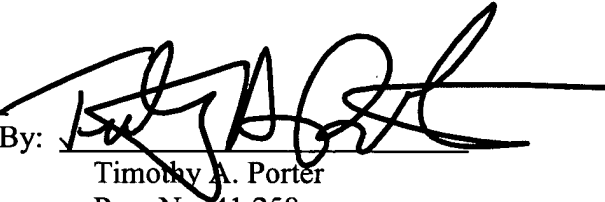
Claims 1, 3-9, 11-14, 19, 21, 23, 29, 37, 39-45, 47-50, 55, 91 and 97-100 were provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 3-7, 9-12, 27-31, 33-36, 55-63, 65-74 and 76-104 of copending Application No. 09/174,856. The applicant notes that this is a provisional rejection, and will submit a terminal disclaimer at such time as the latter claims have been patented.

4. Conclusion

The applicant submits that all claims are now in condition for allowance. Please charge the fee of \$120.00 for a one month extension to Deposit Account 50-0496. Should any other charges be due, the Commissioner is authorized to charge the above-referenced deposit account.

Respectfully submitted,

Date: 5/19/06

By: 

Timothy A. Porter
Reg. No. 41,258
Attorney for Applicant

Symyx Technologies, Inc.
3100 Central Expressway
Santa Clara, CA 95051
Phone: (408) 720-2523; Fax: (408) 773-4029